

Appl. No.: 10/690,462

Amendment dated August 24, 2005

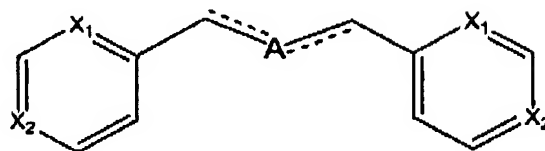
Reply to Office Action of February 25, 2005

Page 2

Amendments to the Claims:

1-12 (Cancelled)

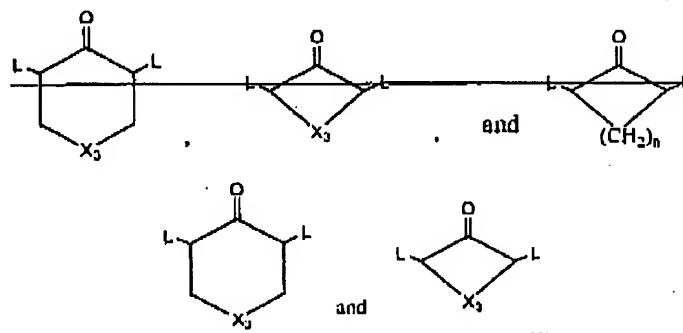
13. (Currently amended) A compound of the formula



wherein:

one of X_1 and X_2 is nitrogen and the other is carbon, wherein each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF_3 , alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, carboxylic acid, carboxylic ester, carboxamide, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

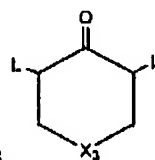
A is selected from the group consisting of:



wherein n is 1-8; X_3 is O, S, SO, SO_2 , or NR_1 ; and R_1 is selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl;

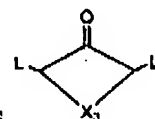
Appl. No.: 10/690,462
Amendment dated August 24, 2005
Reply to Office Action of February 25, 2005
Page 3

the dashed lines indicate the presence of optional double bonds;
L is the point of bonding of A to the compound structure; ~~and or~~
a pharmaceutically acceptable salt thereof.



14. (Previously presented) The compound of Claim 13, wherein A is

15. (Previously presented) The compound of Claim 14, wherein X_3 is S or NR_1 .



16. (Previously presented) The compound of Claim 13, wherein A is

17. (Cancelled)

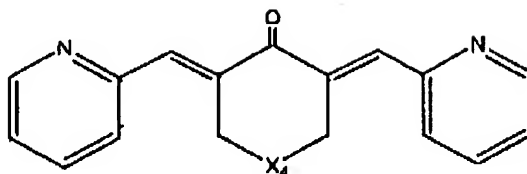
18. (Previously presented) The compound of Claim 13, wherein X_1 is nitrogen.

19. (Previously presented) The compound of Claim 13, wherein X_2 is nitrogen.

20. (Previously presented) The compound of Claim 13, wherein the optional double bonds are present.

21. (Currently amended) The compound of Claim 13, having the formula

Appl. No.: 10/690,462
 Amendment dated August 24, 2005
 Reply to Office Action of February 25, 2005
Page 4



wherein:

X_4 is NR_1 ;

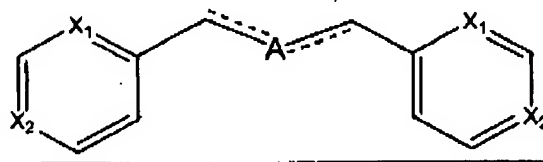
R_1 is selected from the group consisting of H, ~~alkyl~~, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl and dialkylaminocarbonyl;

each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF_3 , alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, carboxylic acid, carboxylic ester, carboxamide, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

and or a pharmaceutically acceptable salts salt thereof.

22. (Currently amended) The compound of Claim 13, ~~selected from the group consisting of~~ wherein the compound is 3,5-Bis-(2-pyridinylidene)-piperidin-4-one, 3,5-Bis-(2-pyridinylidene)-1-methylpiperidin-4-one, and 3,5-Bis-(4-pyridinylidene)-1-methylpiperidin-4-one.

23. (Currently amended) A pharmaceutical formulation, comprising a compound of claim 13 the formula



wherein:

one of X_1 and X_2 is nitrogen and the other is carbon, wherein each carbon atom of

Appl. No.: 10/690,462

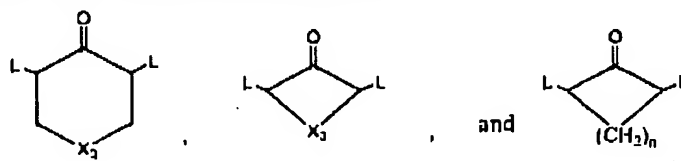
Amendment dated August 24, 2005

Reply to Office Action of February 25, 2005

Page 5

the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF₃, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, carboxylic acid, carboxylic ester, carboxamide, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

A is selected from the group consisting of:



wherein n is 1-8; X₃ is O, S, SO, SO₂, or NR₁; and R₁ is selected from the group consisting of H, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxy carbonyl, aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl;

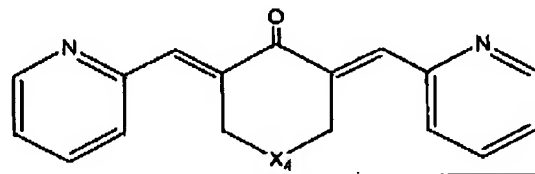
the dashed lines indicate the presence of optional double bonds;

L is the point of bonding of A to the compound structure; or

a pharmaceutically acceptable salt thereof;

and a pharmaceutically acceptable carrier.

24. (Currently amended) A pharmaceutical formulation according to claim 23, comprising a compound of ~~Claim 24~~ the formula



wherein:

X₄ is NR₁;

Appl. No.: 10/690,462
 Amendment dated August 24, 2005
 Reply to Office Action of February 25, 2005
 Page 6

R₁ is selected from the group consisting of H, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxy carbonyl, aminocarbonyl, alkylaminocarbonyl and dialkylaminocarbonyl;

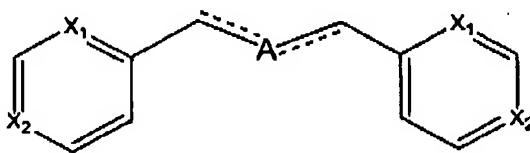
each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF₃, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, carboxylic acid, carboxylic ester, carboxamide, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

or a pharmaceutically acceptable salt thereof;

and a pharmaceutically acceptable carrier.

25. (Currently amended) A pharmaceutical formulation according to claim 23, comprising a compound of Claim 22 3-5-Bis-(2-pyridinylidene)-piperidin-4-one, and a pharmaceutically acceptable carrier.

26. (Currently amended) A method of treating cancerous tissue in a subject, comprising administering to the subject an effective amount of a compound of formula



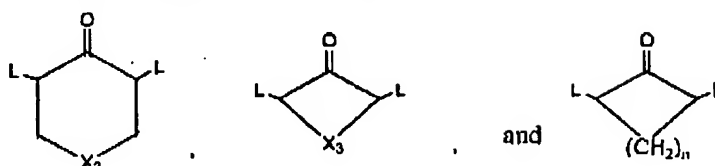
wherein:

one of X₁ and X₂ is nitrogen and the other is carbon, wherein each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF₃, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, carboxylic acid, carboxylic ester, carboxamide, nitro, cyano, azide,

Appl. No.: 10/690,462
 Amendment dated August 24, 2005
 Reply to Office Action of February 25, 2005
 Page 7

alkylcarbonyl, acyl, and trialkylammonium;

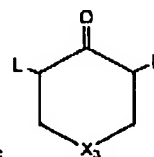
A is selected from the group consisting of:



wherein n is 1-8; X₃ is O, S, SO, SO₂, or NR₁; and R₁ is selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl;

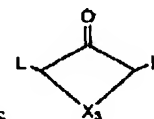
the dashed lines indicate the presence of optional double bonds;

L is the point of bonding of A to the compound structure; and or
a pharmaceutically acceptable salt thereof.

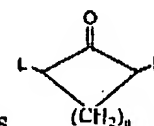


27. (Previously presented) The method of Claim 26, wherein A is

28. (Previously presented) The method of Claim 27, wherein X₃ is S or NR₁.



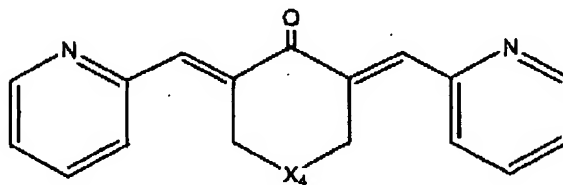
29. (Previously presented) The method of Claim 26, wherein A is



30. (Previously presented) The method of Claim 26, wherein A is 4.

Appl. No.: 10/690,462
Amendment dated August 24, 2005
Reply to Office Action of February 25, 2005
Page 8

31. (Previously presented) The method of Claim 26, wherein X_1 is nitrogen.
32. (Previously presented) The method of Claim 26, wherein X_2 is nitrogen.
33. (Previously presented) The method of Claim 26, wherein the optional double bonds are present.
34. (Currently amended) The method of Claim 26, wherein the compound has the formula



wherein:

X_4 is NR_1 ;

R_1 is selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl and dialkylaminocarbonyl;

each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF_3 , alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, carboxylic acid, carboxylic ester, carboxamide, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

and or a pharmaceutically acceptable ~~salt~~ salt thereof.

35. (Previously presented) The method of Claim 26, wherein the compound is selected from the group consisting of 3,5-Bis-(2-pyridinylidene)-piperidin-4-one, 3,5-Bis-(2-pyridinylidene)-1-

Appl. No.: 10/690,462
Amendment dated August 24, 2005
Reply to Office Action of February 25, 2005
Page 9

methylnpiperidin-4-one, and 3,5-Bis-(4-pyridinylidene)-1-methylnpiperidin-4-one.

36. (Previously presented) A method of Claim 26, wherein the effective amount comprises an amount sufficient to inhibit VEGF production in the cancerous tissue.

37. (Previously presented) A method of Claim 26, wherein the effective amount comprises an amount sufficient to inhibit TF production in the cancerous tissue.

38. (Previously presented) A method of Claim 26, wherein said administering step comprises administering an effective amount of the compound in a pharmaceutically acceptable carrier.